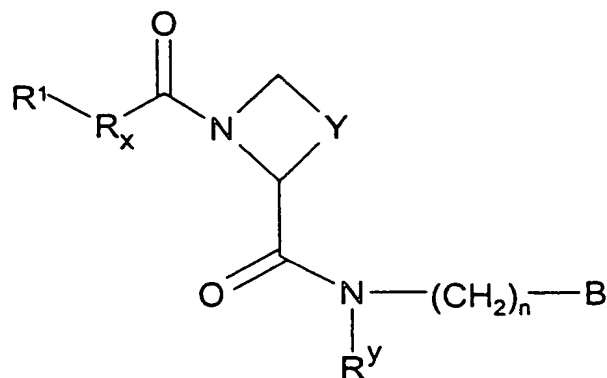


## Claims

1. A compound of formula I,



5

wherein

R<sup>1</sup> represents H, C<sub>1-4</sub> alkyl (optionally substituted by one or more  
 10 substituents selected from cyano, halo, OH, C(O)OR<sup>1a</sup> or C(O)N(R<sup>1b</sup>)R<sup>1c</sup>)  
 or OR<sup>1d</sup>;

R<sup>1d</sup> represents H, C(O)R<sup>11</sup>, SiR<sup>12</sup>R<sup>13</sup>R<sup>14</sup> or C<sub>1-6</sub> alkyl, which latter group is  
 optionally substituted or terminated by one or more substituent selected  
 from OR<sup>15</sup> or (CH<sub>2</sub>)<sub>q</sub>R<sup>16</sup>;

15 R<sup>12</sup>, R<sup>13</sup> and R<sup>14</sup> independently represent H, phenyl or C<sub>1-6</sub> alkyl;

R<sup>16</sup> represents C<sub>1-4</sub> alkyl, phenyl, OH, C(O)OR<sup>17</sup> or C(O)N(H)R<sup>18</sup>;

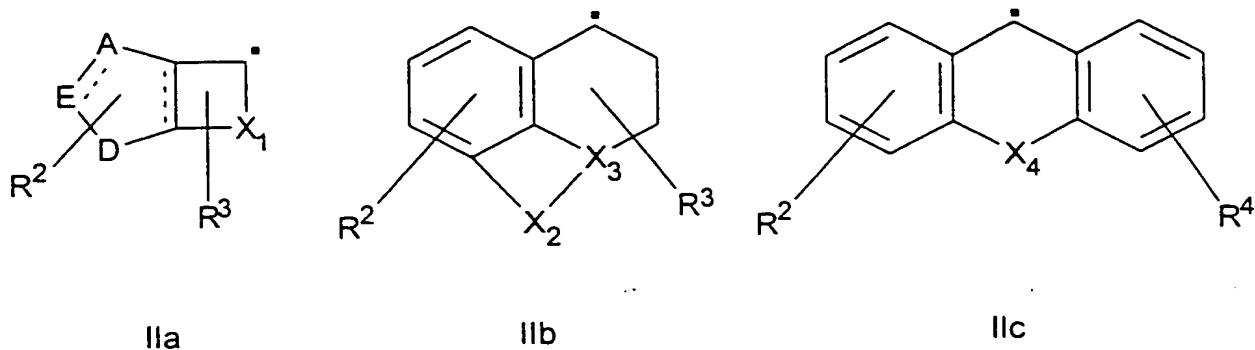
R<sup>18</sup> represents H, C<sub>1-4</sub> alkyl or CH<sub>2</sub>C(O)OR<sup>19</sup>;

R<sup>15</sup> and R<sup>17</sup> independently represent H, C<sub>1-6</sub> alkyl or C<sub>1-3</sub> alkylphenyl;

R<sup>1a</sup>, R<sup>1b</sup>, R<sup>1c</sup>, R<sup>11</sup> and R<sup>19</sup> independently represent H or C<sub>1-4</sub> alkyl; and

20 q represents 0, 1 or 2;

$R_x$  represents a structural fragment of formula IIa, IIb or IIc,



5 wherein

the dotted lines independently represent optional bonds;

A and E independently represent O or S, CH or CH<sub>2</sub> (as appropriate), or N or N(R<sup>21</sup>) (as appropriate);

D represents -CH<sub>2</sub>-, O, S, N(R<sup>22</sup>), -(CH<sub>2</sub>)<sub>2</sub>-, -CH=CH-, -CH<sub>2</sub>N(R<sup>22</sup>)-,

10 -N(R<sup>22</sup>)CH<sub>2</sub>-, -CH=N-, -N=CH-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, -CH<sub>2</sub>S- or -SCH<sub>2</sub>-;

X<sub>1</sub> represents C<sub>2-4</sub> alkylene; C<sub>2-3</sub> alkylene interrupted by Z; -C(O)-Z-A<sup>1</sup>-;

-Z-C(O)-A<sup>1</sup>-; -CH<sub>2</sub>-C(O)-A<sup>1</sup>-; -Z-C(O)-Z-A<sup>2</sup>-; -CH<sub>2</sub>-Z-C(O)-A<sup>2</sup>-;

-Z-CH<sub>2</sub>-C(O)-A<sup>2</sup>-; -Z-CH<sub>2</sub>-S(O)<sub>m</sub>-A<sup>2</sup>-; -C(O)-A<sup>3</sup>-; -Z-A<sup>3</sup>-; or -A<sup>3</sup>-Z-;

X<sub>2</sub> represents C<sub>2-3</sub> alkylene, -C(O)-A<sup>4</sup>- or -A<sup>4</sup>-C(O)-;

15 X<sub>3</sub> represents CH or N;

X<sub>4</sub> represents a single bond, O, S, C(O), N(R<sup>23</sup>), -CH(R<sup>23</sup>)-,

-CH(R<sup>23</sup>)-CH(R<sup>24</sup>)- or -C(R<sup>23</sup>)=C(R<sup>24</sup>)-;

A<sup>1</sup> represents a single bond or C<sub>1-2</sub> alkylene;

A<sup>2</sup> represents a single bond or -CH<sub>2</sub>-;

20 A<sup>3</sup> represents C<sub>1-3</sub> alkylene;

A<sup>4</sup> represents C(O) or C<sub>1-2</sub> alkylene;

Z represents, at each occurrence, O, S(O)<sub>m</sub> or N(R<sup>25</sup>);

R<sup>2</sup> and R<sup>4</sup> independently represent one or more optional substituents

selected from  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy (which latter two groups are optionally substituted by one or more halo substituent), methylenedioxy, halo, hydroxy, cyano, nitro,  $S(O)_2NH_2$ ,  $C(O)OR^{26}$ ,  $SR^{26}$ ,  $S(O)R^{26a}$ ,  $S(O)_2R^{26a}$  or  $N(R^{27})R^{28}$ ;

- 5  $R^3$  represents one or more optional substituents selected from OH,  $C_{1-4}$  alkoxy,  $C_{1-6}$  alkyl (optionally substituted by one or more halo group), or  $N(R^{29a})R^{29b}$ ;

$R^{25}$ ,  $R^{29a}$  and  $R^{29b}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ ;

$R^{26}$  represents H or  $C_{1-4}$  alkyl;

- 10  $R^{26a}$  represents  $C_{1-4}$  alkyl;

$R^{27}$  and  $R^{28}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ , or together represent  $C_{3-6}$  alkylene, thus forming a 4- to 7-membered ring, which ring is optionally substituted, on a carbon atom that is  $\alpha$  to the nitrogen atom, with an =O group;

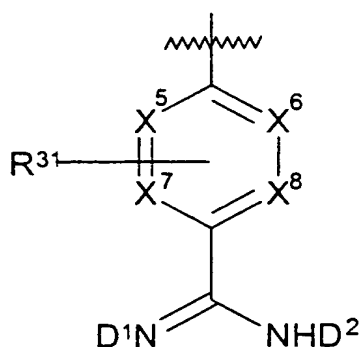
- 15  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$  and  $R^{30}$  independently represent, at each occurrence, H or  $C_{1-4}$  alkyl;

- Y represents  $CH_2$ ,  $(CH_2)_2$ ,  $CH=CH$  (which latter group is optionally substituted by  $C_{1-4}$  alkyl),  $(CH_2)_3$ ,  $CH_2CH=CH$  or  $CH=CHCH_2$  (which latter three groups are optionally substituted by  $C_{1-4}$  alkyl, methylene, =O or hydroxy);
- 20

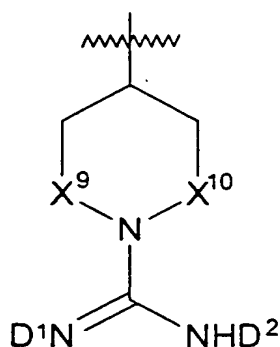
$R^y$  represents H or  $C_{1-4}$  alkyl;

- 25 n represents 0, 1, 2, 3 or 4; and

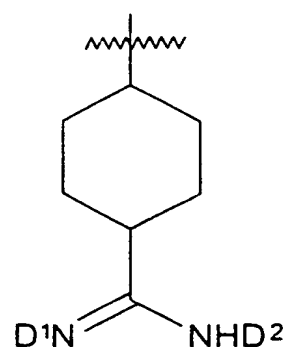
B represents a structural fragment of formula IIIa, IIIb or IIIc



IIIa



IIIb



IIIc

wherein

$X^5$ ,  $X^6$ ,  $X^7$  and  $X^8$  independently represent CH, N or N-O;

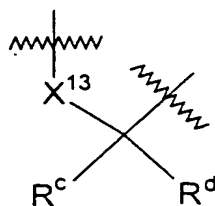
$X^9$  and  $X^{10}$  independently represent a single bond or  $CH_2$ ;

- 5  $R^{31}$  represents an optional substituent selected from halo,  $C_{1-4}$  alkyl (which group is optionally substituted by one or more halo group),  $N(R^{32})R^{33}$ ,  $OR^{34}$  or  $SR^{35}$ ;

$R^{32}$  and  $R^{33}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{36}$ ;

$R^{34}$ ,  $R^{35}$  and  $R^{36}$  independently represent H or  $C_{1-4}$  alkyl; and

- 10 one of  $D^1$  and  $D^2$  represents H, and the other represents H,  $OR^a$ ,  $NHR^a$ ,  $C(=X^{11})X^{12}R^b$ , or  $D^1$  and  $D^2$  together represent a structural fragment of formula IVa:-



IVa

$R^a$  represents H or  $-A^5[X^{14}]_n[C(O)]_rR^c$ ;

- 15  $R^b$  represents  $-A^5[X^{14}]_n[C(O)]_rR^c$ ;

$A^5$  represents, at each occurrence, a single bond or  $C_{1-12}$  alkylene (which alkylene group is optionally interrupted by one or more O,  $S(O)_m$  and/or

- N(R<sup>f</sup>) group, and is optionally substituted by one or more of halo, OH, N(H)C(O)R<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup>, C<sub>3-7</sub>-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group and/or is optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, halo, =O or =S), Het and C<sub>6-10</sub> aryl (which aryl and Het groups are themselves optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl (optionally substituted by one or more halo substituent), C<sub>1-6</sub> alkoxy, halo, cyano, C(O)OR<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup> and N(R<sup>f</sup>)R<sup>g</sup>);
- 10 R<sup>c</sup> and R<sup>d</sup> both represent H; or one of R<sup>c</sup> and R<sup>d</sup> represents H or C<sub>1-7</sub> alkoxy and the other represents C<sub>1-7</sub> alkyl (which alkyl group is optionally interrupted by one or more O atoms); or R<sup>c</sup> and R<sup>d</sup> together represent C<sub>3-8</sub> cycloalkyl, which cycloalkyl group is interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group;
- 15 R<sup>e</sup> represents, at each occurrence, H, C<sub>1-12</sub> alkyl (which alkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group, and/or is optionally substituted by one or more substituents selected from halo, OH, N(H)C(O)R<sup>g</sup> and C(O)N(R<sup>g</sup>)R<sup>h</sup>), A<sup>7</sup>-C<sub>3-7</sub>-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or
- 20 N(R<sup>f</sup>) group and/or is substituted by one or more substituents selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, halo, =O and =S), A<sup>7</sup>-C<sub>6-10</sub> aryl or A<sup>7</sup>-Het (which aryl and Het groups are optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl (optionally substituted by one or more halo substituent), C<sub>1-6</sub> alkoxy, halo, cyano, C(O)OR<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup> and
- 25 N(R<sup>f</sup>)R<sup>g</sup>);
- A<sup>7</sup> represents a single bond or C<sub>1-7</sub> alkylene (which alkylene group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group, and/or are optionally substituted by one or more of halo, OH, N(H)COR<sup>g</sup> and CON(R<sup>g</sup>)R<sup>h</sup>);

Het represents, at each occurrence, a five- to ten-membered heteroaryl group, which may be aromatic in character, containing one or more nitrogen, oxygen or sulphur atoms in the ring system;

n and r independently represent 0 or 1;

5  $X^{11}$ ,  $X^{12}$  and  $X^{14}$  independently represent O or S;

$X^{13}$  represents O or  $N(R^f)$ ;

$R^f$  represents, at each occurrence, H,  $C_{1-4}$  alkyl or  $C(O)R^g$ ;

$R^g$  and  $R^h$  independently represent, at each occurrence, H or  $C_{1-4}$  alkyl;  
and

10

m represents, at each occurrence, 0, 1 or 2;

or a pharmaceutically acceptable salt thereof;

15 provided that:

(a) A and E do not both represent O or S;

(b) E and D do not both represent O or S;

(c) when  $R^1$  represents  $OR^{1d}$  and  $X_1$  represents  $-C(O)-Z-A^1$ ,  
- $Z-CH_2-S(O)_m-A^2$ - or  $-Z-C(O)-Z-A^2$ , then  $A^1$  or  $A^2$  (as appropriate) do not  
20 represent a single bond;

(f) when  $X_4$  represents  $-CH(R^{23})-$ ,  $R^1$  does not represent OH;

(g) when  $A^5$  represents a single bond, then n and r both represent 0;

(f) when  $A^5$  represents  $C_{1-12}$  alkylene, then n represents 1;

(g) when  $A^5$  represents  $-CH_2-$ , n is 1 and r is 0, then  $R^c$  does not represent

25 H; and

(h) the compound is not:-

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(R)- or (S)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

- (*R*)- or (*S*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab;  
 1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 1-hydroxy-5,7-dimethyltetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 5 1-hydroxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 (*R*)- or (*S*)-7-methoxy-1-methyltetralin-1-yl-C(O)-Aze-Pab;  
 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x OAc;  
 (*S*)- or (*R*)-1-hydroxy-4-methoxyindan-1-yl-C(O)-Aze-Pab;  
 10 1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);  
 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OH);  
 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OMe);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-  
 15 (C(O)OCH<sub>2</sub>CCl<sub>3</sub>);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-  
 (C(O)OCH<sub>2</sub>CH<sub>3</sub>);  
 7-methoxy-1-allyltetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 (*S*)- or (*R*)-1-hydroxy-7-chlorotetralin-1-yl-C(O)-Pro-Pab;  
 20 1-*n*-propyl-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
 6-chloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
 4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
 6,8-dichloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
 6-fluoro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
 25 4-hydroxy-6-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
 8-chloro-4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
 6-chloro-4-hydroxy-8-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-*i*-Pr);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Et);

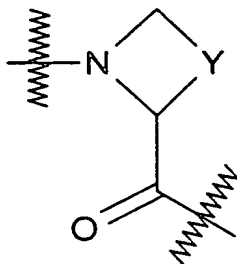
- (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Ch);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-allyl);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Bzl);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-  
 5 (CO-O-methallyl);  
 1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab(OH);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Val);  
 (*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-(Me)Pab; or  
 9-hydroxyfluoren-9-yl-C(O)-Aze-Pab x HOAc.
- 10
2. A compound as claimed in Claim 1 wherein R<sup>1</sup> represents OH or C<sub>1-4</sub> alkyl (which latter group is optionally substituted by cyano or OH).
3. A compound as claimed in any one of the preceding claims wherein R<sub>x</sub>  
 15 represents a structural fragment of formula IIa or IIb.
4. A compound as claimed in any one of the preceding claims wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, then the dotted lines represent bonds, A and E both represent CH and D represents  
 20 -CH=CH-;
5. A compound as claimed in any one of the preceding claims wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, X<sub>1</sub> represents optionally unsaturated C<sub>2</sub>- or C<sub>3</sub>-alkylene, or -Z-A<sup>3</sup> (in which Z represents  
 25 O, S(O)<sub>m</sub> or N(R<sup>25</sup>) (in which R<sup>25</sup> is as defined in Claim 1 or represents C<sub>1-4</sub> alkyl or C(O)R<sup>30</sup> and m and R<sup>30</sup> are as defined in Claim 1) and A<sup>3</sup> represents C<sub>1</sub>- or C<sub>2</sub>-alkylene (which latter group is optionally unsaturated)).



6. A compound as claimed in any one of the preceding claims wherein Y represents  $\text{CH}_2$ ,  $(\text{CH}_2)_2$  or  $(\text{CH}_2)_3$ .
7. A compound as claimed in any one of the preceding claims wherein B  
5 represents a structural fragment of formula IIIa in which  $\text{X}^5$ ,  $\text{X}^6$ ,  $\text{X}^7$  and  $\text{X}^8$  all represent CH.
8. A compound as claimed in any one of the preceding claims wherein,  
when  $\text{D}^1$  and  $\text{D}^2$  together represent a structural fragment of formula IVa,  
10 in which  $\text{X}^{13}$  is O, then one of  $\text{R}^c$  and  $\text{R}^d$  represents H or  $\text{C}_{1-7}$  alkoxy and the other represents  $\text{C}_{1-7}$  alkyl.
9. A compound as claimed in any one of Claims 1 to 7, wherein, when  $\text{D}^1$  or  $\text{D}^2$  represents  $\text{OR}^a$  and  $\text{R}^a$  represents  $-\text{A}^5[\text{X}^{14}]_n[\text{C}(\text{O})]_r\text{R}^e$ , and  
15 (i)  $\text{A}^5$  is a single bond, then  $\text{R}^e$  is:-  
(1)  $\text{A}^7$ -aryl, optionally substituted by one or more halo,  $\text{C}_{1-6}$  alkoxy,  $\text{C}_{1-6}$  alkyl or halo- $\text{C}_{1-6}$ -alkyl substituents; or  
(2) H or linear, branched, optionally unsaturated, and/or cyclic,  $\text{C}_{1-12}$  alkyl, which cyclic alkyl group is optionally interrupted by an O  
20 atom and, optionally, a further O atom or  $\text{S}(\text{O})_m$  group; or when  
(ii)  $\text{A}^5$  is linear or branched  $\text{C}_{1-12}$  alkylene,  $\text{X}^{14}$  is O and r is 0, then  $\text{R}^e$  is  $\text{C}_{1-3}$  alkyl or  $\text{A}^7$ -aryl, in which  $\text{A}^7$  is a single bond.
10. A compound as claimed in any one of Claims 1 to 7 or 9, wherein,  
25 when  $\text{D}^1$  or  $\text{D}^2$  represents  $\text{OR}^a$ , then  $\text{R}^a$  is H or  $\text{C}_{1-4}$  alkyl.
11. A compound as claimed in any one of Claims 1 to 7, wherein, when  $\text{D}^1$  or  $\text{D}^2$  represents  $-\text{C}(=\text{X}^{11})\text{X}^{12}\text{R}^b$ , in which  $\text{X}^{11}$  represents O and  $\text{X}^{12}$  represents O or S, and, in which  $\text{R}^b$  group,  $\text{A}^5$  represents a single bond.

then R<sup>c</sup> represents optionally unsaturated C<sub>1-6</sub> alkyl, A<sup>7</sup>-C<sub>6-10</sub>-aryl (in which A<sup>7</sup> represents a single bond or C<sub>1-2</sub> alkylene, and which A<sup>7</sup>-C<sub>6-10</sub>-aryl group is optionally substituted by one or more halo, C<sub>1-4</sub> alkyl and/or C<sub>1-4</sub> alkoxy groups), or A<sup>7</sup>-C<sub>3-7</sub>-cycloalkyl, in which A<sup>7</sup> represents a single bond or  
 5 linear or branched C<sub>1-7</sub> alkylene, and which cycloalkyl group is optionally substituted by C<sub>1-3</sub> alkyl.

12. A compound of formula I, as defined in any one of the preceding claims, wherein the fragment



10

is in the S-configuration.

13. A pharmaceutical formulation including a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, in  
 15 admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

20 15 A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition where inhibition of thrombin is required.

16. A compound as defined in any one of Claims 1 to 12, or a  
 25 pharmaceutically acceptable salt thereof, for use in the treatment of.

thrombosis.

17. A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

5

18. The use of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

10

19. The use as claimed in Claim 18, wherein the condition is thrombosis.

20. The use of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an anticoagulant.

15

21. A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

20

22. A method as claimed in Claim 21, wherein the condition is thrombosis.

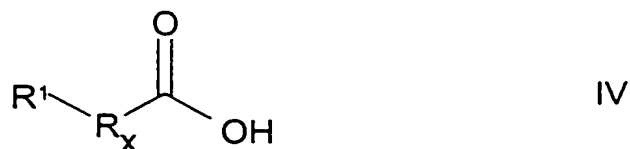
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23. A method as claimed in Claim 21, wherein the condition is hypercoagulability in blood and tissues.

24. A process for the preparation of compounds of formula I which

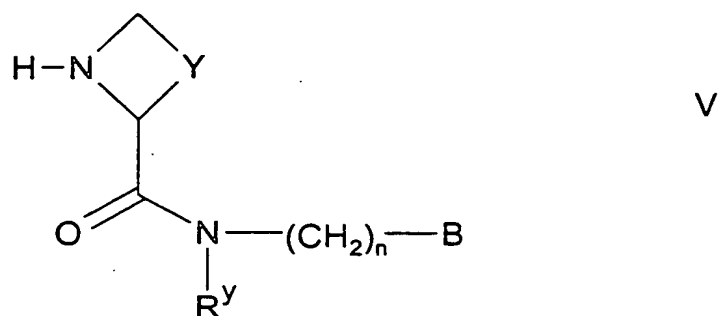
comprises:

(i) the coupling of a compound of formula IV,



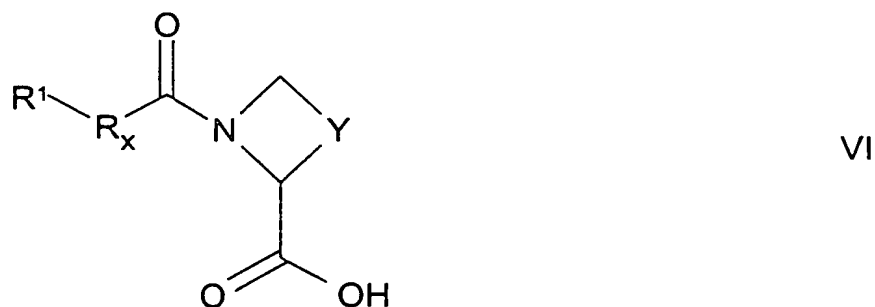
wherein  $\text{R}^1$  and  $\text{R}_x$  are as defined in Claim 1 with a compound of formula

5 V,



wherein  $\text{R}^y$ , Y, n and B are as defined in Claim 1;

(ii) the coupling of a compound of formula VI,



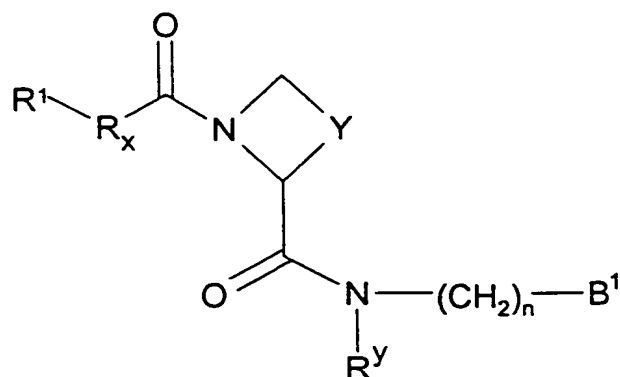
10 wherein  $\text{R}^1$ ,  $\text{R}_x$  and Y are as defined in Claim 1 with a compound of formula VII,



wherein  $\text{R}^y$ , n and B are as defined in Claim 1;

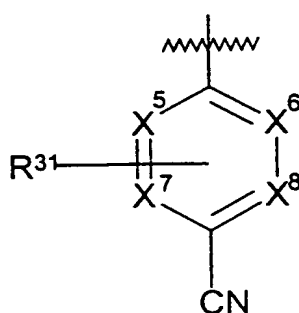
(iii) for compounds of formula I in which  $\text{D}^1$  or  $\text{D}^2$  represents  $\text{OR}^a$  or

15  $\text{NHR}^a$ , reaction of a compound of formula VIII,

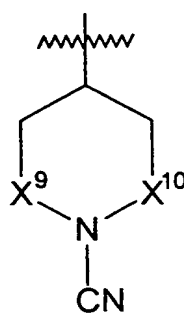


VIII

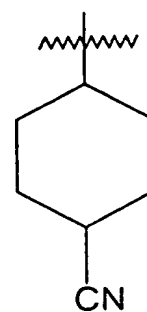
wherein B<sup>1</sup> represents a structural fragment of formula IIIId, IIIe or IIIf



IIIId



IIIe



IIIIf

and R<sup>1</sup>, R<sub>x</sub>, Y, R<sup>y</sup>, n, R<sup>31</sup>, X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup>, X<sup>8</sup>, X<sup>9</sup> and X<sup>10</sup> are as defined in

5 Claim 1 with a compound of formula IX,



IX

wherein X<sup>a</sup> represents O or NH and R<sup>a</sup> is as defined in Claim 1;

(iv) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup> or NHR<sup>a</sup>, reaction of a compound of formula I in which D<sup>1</sup> or D<sup>2</sup> (as  
10 appropriate) represents C(O)OR<sup>b1</sup>, in which R<sup>b1</sup> represents a protecting group with a compound of formula IX as defined above;

(v) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup> or NHR<sup>a</sup>, R<sup>a</sup> represents -A<sup>5</sup>[X<sup>14</sup>]<sub>n</sub>[C(O)]<sub>r</sub>R<sup>c</sup>, in which A<sup>5</sup> does not represent a single bond, and n represent 1, reaction of a compound of formula I in  
15 which D<sup>1</sup> or D<sup>2</sup> (as appropriate) represents OH or NH<sub>2</sub>, with a compound

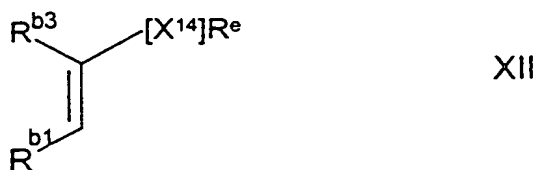
of formula X,



wherein  $L^1$  represents a suitable leaving group,  $A^{5a}$  represents  $A^5$ , as defined in Claim 1 except that it does not represent a single bond, and  $X^{14}$ ,

5  $r$  and  $R^c$  are as defined in Claim 1;

(vi) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^c$ , in which  $A^5$  represents  $C_{2-12}$  alkylene, which alkylene group is branched at the carbon atom that is  $\alpha$  to the O or N atom of  $OR^a$  or  $NHR^a$  (as appropriate), and which group is  
10 optionally branched at the carbon atom that is  $\beta$  to that atom,  $n$  represents 1,  $r$  represents 0 and  $R^c$  is as defined in Claim 1, reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents OH or  $NH_2$ , with a compound of formula XI,



15 or a geometrical isomer thereof, or a mixture of such geometrical isomers, in which  $R^{b1}$  and  $R^{b3}$  each represent H or an alkyl group, provided that the total number of carbon atoms provided by  $R^{b1}$  and  $R^{b3}$  does not exceed 10, and wherein  $X^{14}$  and  $R^c$  are as defined in Claim 1;

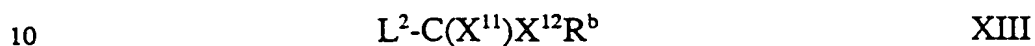
(vii) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  
20  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^c$ , in which  $A^5$  represents a single bond, and  $R^c$  represents  $A^7-C_{3-6}$ -cycloalkyl, in which  $A^7$  represents a single bond, and the cycloalkyl group is interrupted by at least one O or S atom, which atom is between the carbon atom at the point of attachment to the O or NH group of  $OR^a$  or  $NHR^a$ , and a carbon atom that is  $\alpha$  to that  
25 point of attachment, and which cycloalkyl group is optionally interrupted by one or more O or  $S(O)_m$  group and/or optionally substituted by one or

more =O group, reaction of a compound of formula I, in which D<sup>1</sup> or D<sup>2</sup> (as appropriate) represents OH or NH<sub>2</sub>, with a compound of formula XII,



wherein X<sup>15</sup> represents O or S and X<sup>16</sup> represents C<sub>1-4</sub> alkylene (which  
5 alkylene group is optionally interrupted by one or more O or S(O)<sub>m</sub> group and/or optionally substituted by one or more =O group);

(viii) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents C(X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, reaction of a compound of formula I in which D<sup>1</sup> and D<sup>2</sup> both represent H with a compound of formula XIII,



wherein L<sup>2</sup> represents a suitable leaving group, and X<sup>11</sup>, X<sup>12</sup> and R<sup>b</sup> are as defined in Claim 1;

(ix) for compounds of formula I in which D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa, reaction of a corresponding compound  
15 of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OH or NHR<sup>f</sup> (in which R<sup>f</sup> is as defined in Claim 1), with a compound of formula XV,



wherein R<sup>c1</sup> and R<sup>c2</sup> both represent -OR<sup>c3</sup>, in which R<sup>c3</sup> represents C<sub>1-3</sub> alkyl, or together represent =O, and R<sup>c</sup> and R<sup>d</sup> are as defined in Claim 1;

(x) for compounds of formula I in which one or more of X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> represent N-O, oxidation of a corresponding compound of formula I in  
20 which X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and/or X<sup>8</sup> (as appropriate) represent(s) N; or

(xi) for compounds of formula I in which any one of Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> comprises or includes a S(O) or a S(O)<sub>2</sub> group,  
25 oxidation of a corresponding compound of formula I (or a compound corresponding to a compound of formula I) wherein Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> (as appropriate) comprise(s) or include(s) a S group;

- (xii) for compounds of formula I in which  $D^1$  and  $D^2$  both represent H, removal of a  $OR^a$ ,  $NHR^a$  or  $C(=X^{11})X^{12}R^b$  group (in which  $R^a$ ,  $R^b$ ,  $X^{11}$  and  $X^{12}$  are as defined in Claim 1), or removal of a structural fragment of formula IVa as defined in Claim 1, from a corresponding compound of formula I; or
- (xiii) introduction and/or interconversion of a substituent on an aromatic and/or non-aromatic, carbocyclic and/or heterocyclic ring in a corresponding compound of formula I.